

Relationship of serum progesterone (P) level the day after human chorionic gonadotropin (hCG) injection on outcome following in vitro fertilization-embryo transfer (IVF-ET)

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Summary

Purpose: To determine if either too little or too much of a rise in serum progesterone (P) on the day after human chorionic gonadotropin (hCG) injection has any negative impact on pregnancy outcome following in vitro fertilization-embryo transfer (IVF-ET). **Methods:** Retrospective review. Three progesterone groups established – low, normal and high. **Results:** There was a significantly higher clinical pregnancy rate in the normal P group vs low or high. There were no significant differences in ongoing delivered pregnancy rates but a trend for higher implantation rates in the normal P group. **Conclusions:** These data are consistent with the hypothesis that either too little or too much P can adversely effect implantation. However, the differences are not of sufficient magnitude to warrant a clinical intervention, e.g., deferring fresh transfer and freezing the embryos for future transfer.

Key words: Progesterone; Implantation rate; Luteal phase; In vitro fertilization.

Introduction

There is evidence that a deficiency of progesterone (P) may be associated with infertility [1, 2]. Supplemental P after the use of follicle maturing drugs improves pregnancy outcome [3]. The majority of in vitro fertilization (IVF) programs used P supplementation after retrieval but before embryo transfer to supplement corpus luteum P production and improve IVF outcome [4-6].

The possibility exists that in some instances the corpora lutea do not secrete sufficient P, and even with the P supplementation, pregnancy does not ensue because of insufficient P. On the other hand there is evidence that excessive P production would advance the implantation window so that if excessive P is generated prior to embryo transfer successful implantation may not occur [7, 8].

The present study evaluated the serum P level the day after the human chorionic gonadotropin (hCG) injection to see if either a relatively low response or an exaggerated response correlates with an inferior pregnancy outcome.

Materials and Methods

Serum P levels were drawn one day after the hCG injection in the a.m. This study evaluated all in vitro fertilization-embryo transfer (IVF-ET) cycles where the serum P was obtained the day after the hCG injection in women age ≤ 39 from 1997 to 2004. Both GnRH agonist and antagonist controlled ovarian hyperstimulation protocols were used.

The distribution of serum P levels post hCG was found and the cut-off for the deciles (10th, 20th, 30th, 40th) percentile was established. In vitro fertilization cycles were classified into three groups: P (ng/ml) levels post hCG < 1.9 (10th percentile), P levels post hCG > 1.9 and < 8.4 (40th percentile), P levels post hCG were > 8.4 . These three groups were considered low, normal and high P levels, respectively.

The cut-off values for the deciles are presented in Table 1. Ovarian stimulation characteristics and embryo transfer outcomes were compared by P group.

Results

The stimulation characteristics analyzed included serum E2, P, FSH, and LH levels on the day of hCG and E2, FSH, and LH levels post hCG, number of embryos fertilized per retrieval, and number of embryos transferred. In each case there was a significant difference in mean value as the P levels increased as seen in Table 2 ($p < .05$, analysis of variance).

Table 1. — Cut-off used for deciles of serum P the day after hCG injection.

Percentile	P (ng/ml)
10	1.90
20	2.40
30	3.00
40	3.60
50	4.20
60	4.90
70	5.70
80	6.80
90	8.40

P: progesterone.

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Table 2. — Comparison of stimulation characteristics by serum P levels.

Characteristics	P	Mean \pm Standard Deviation	p value (analysis of variance)
E2 day of hCG (pg/ml)	1	878.5 \pm 752.8	.000
	2	2312.1 \pm 1141.0	
	3	3846.0 \pm 1725.9	
P day of hCG (ng/ml)	1	.7 \pm .4	.000
	2	1.4 \pm .9	
	3	2.2 \pm 1.4	
LH day of hCG (IU/ml)	1	4.4 \pm 4.0	.000
	2	3.8 \pm 3.4	
	3	2.5 \pm 2.0	
FSH day of hCG	1	19.8 \pm 11.1	.000
	2	17.7 \pm 9.4	
	3	13.5 \pm 6.4	

P: progesterone.

1 = low P group; 2 = normal P group; 3 = high P group.

Table 3. — Comparison of outcome variables.

Outcome	P group	p value (chi-square)
Clinical pregnancy rate/transfer	1	34.6% (56/162)
	2	43.5% (492/1132)
	3	35.5% (49/138)
Ongoing/delivered pregnancy rate/transfer	1	32.7% (53/162)
	2	38.1% (431/1132)
	3	34.1% (47/138)
Implantation rate	1	18.1% (76/419)
	2	22.2% (761/3425)
	3	19.5% (84/431)

1 = low P group; 2 = normal P group; 3 = high P group.

The clinical pregnancy rates in P groups 1 and 3 were significantly lower than group 2 as seen in Table 3 ($p < .05$, chi-square analysis). The outcome variables, ongoing/delivered pregnancy rates and implantation rates, however, did not differ by P groups as seen in Table 3 ($p = \text{NS}$, chi-square analysis).

Conclusion

The significant difference in clinical pregnancy rates and the trend for a difference in implantation rates in groups 1 and 3 vs 2 is consistent with the hypothesis that too little or too much of a P response the day after hCG may have a negative effect on potential embryo implantation. However, the differences are not sufficient to be clinically important.

It would not seem prudent for example to purposely cryopreserve all embryos and defer fresh embryo transfer because of an insufficient or excessive rise in P the day after hCG.

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